

Appl. No. : 10/033,167
Filed : December 27, 2001

REMARKS

Applicants have amended Claim 27 to recite the limitation that the claimed isolated nucleic acid is amplified at least 2-fold in colon tumor cells or lung tumor cells compared to normal colon cells or normal lung cells, respectively; or said isolated nucleic acid encodes a polypeptide which is expressed in colon tumor cells or lung tumor cells at levels at least 2-fold higher than levels in normal colon cells or normal lung cells, respectively. Applicants maintain that the amendments add no new matter and are fully supported by the specification as originally filed. For example, support for the amendments to Claim 27 can be found in Example 16 beginning at page 111, line 35, through page 117, line 51, particularly page 111, line 37, through line page 112, line 3, and Table 7 (Table 8 as amended) on page 117 of the specification.

Claims 27, 28 and 32-34 are presented for examination. Applicants respond below to the specific rejections raised by the Examiner in the Office Action mailed September 30, 2004. For the reasons set forth below, Applicants respectfully traverse.

Rejections under 35 U.S.C. § 112, first paragraph – Written Description

The PTO has rejected Claims 27, 28, 32-34 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one of skill in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

The PTO argues that the use of “hybridization” language causes the claims to include variants for which no written description is provided since there is no description of any other sequence besides SEQ ID NO: 7 which “hybridize” to SEQ ID NO: 7. The PTO argues that there are no common elements or attributes of the sequence disclosed, and there are no structural limitations or requirements which provide guidance on the identification of sequences which would meet these functional limitations.

The PTO also argues that the claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific amino acid sequences have been provided. The PTO states that no written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

Appl. No. : 10/033,167
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The PTO notes that while Example 9 of the [written description] guidelines reads stringent hybridization conditions as yielding less variation, in this case the variations are significant because there is no expectation that other sequences which hybridize to SEQ ID NO: 7 would themselves hybridize to targets which are overexpressed in cancer cells, which the PTO states is the asserted utility of SEQ ID NO: 7.

The PTO asserts that while variants of SEQ ID NO: 7 are likely to exist, except for SEQ ID NO: 7, there is a “complete absence of knowledge as to what sequence comprises these variants.” Office Action at 3. Citing *Regents of University of California v. Eli Lilly and Co.*, 34 USPQ2d 1398 (Fed Cir. 1997), the PTO states that this is a situation of naming a type of material which is generally known to likely exist, but, except for SEQ ID NO: 7 itself, in the absence of knowledge of the material composition, fails to provide descriptive support for the generic claim to anything which hybridizes to SEQ ID NO: 7 under stringent conditions.

Finally, the PTO states that there is no conception of sequences which hybridize to SEQ ID NO: 7 except by the functional utility of “hybridization,” and that Applicant has no definition of the structure of these molecules or of any structural element relating to these molecules whatsoever. The PTO concludes that the entire claim is functionally drawn to claim compounds which Applicant does not have, which Applicant has not made, and which comprise specific sequences Applicant does not know.

In response to Applicants arguments filed August 24, 2004, the PTO states that the in the absence of a structure function relationship and a representative number of species, there is insufficient descriptive support for the current claims.

Applicants respectfully disagree.

The Legal Standard for Written Description

The well-established test for sufficiency of support under the written description requirement of 35 U.S.C. §112, first paragraph is whether the disclosure “reasonably conveys to artisan that the inventor had possession at that time of the later claimed subject matter.” *In re Kaslow*, 707 F.2d 1366, 1375, 2121 USPQ 1089, 1096 (Fed. Cir. 1983); see also *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991). The adequacy of written description support is a factual issue and is to be determined on a case-by-case basis. See e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991). The factual

Appl. No. : 10/033,167
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determination in a written description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. *Union Oil v. Atlantic Richfield Co.*, 208 F.3d 989, 996 (Fed. Cir. 2000).

The Current Invention is Adequately Described

Applicants initially note the claims are directed in part to nucleic acid molecules that hybridize under specified highly stringent conditions to a complement of a nucleic acid which encodes the *polypeptide* of SEQ ID NO: 7. Applicants assume that the PTO's reference to nucleic acids which hybridize to SEQ ID NO: 7, or nucleic acids of SEQ ID NO: 7, are simple oversight. SEQ ID NO: 6 is one example of a sequence which encodes the polypeptide of SEQ ID NO: 7. One of skill in the art would know how to make other nucleic acid sequences which encode the polypeptide of SEQ ID NO: 7 based on codon degeneracy. Thus, given that Applicants have disclosed SEQ ID NO: 7, what constitutes a complement of a nucleic acid sequence which encodes the polypeptide of SEQ ID NO: 7 would be understood by one of skill in the art.

Applicants also address the PTO's argument that the claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and that only specific amino acid sequences have been provided. The pending claims are directed to isolated nucleic acids which hybridize under the specified conditions to a complement of a nucleic acid sequence encoding the polypeptide of SEQ ID NO:7; the complement of a nucleic acid sequence of SEQ ID NO:6; a complement of the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:6; or a complement of the full-length coding sequence of the cDNA deposited under ATCC accession number 203661. Each of the target sequences are adequately described in the specification. Applicants submit that the pending claims relate to nucleic acids which hybridize to the nucleic acids listed in the claims, not alternately spliced versions of the proteins, allelic variants including insertions and mutations, or inactive precursor proteins which have a removable amino terminal end.

Applicants have amended the claims to include the limitation "wherein said isolated nucleic acid is amplified at least 2-fold in colon tumor cells or lung tumor cells compared to normal colon cells or normal lung cells, respectively; or wherein said isolated nucleic acid

Appl. No. : 10/033,167
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encodes a polypeptide which is expressed in colon tumor cells or lung tumor cells at levels at least 2-fold higher than levels in normal colon cells or normal lung cells, respectively.”

Applicants submit they have addressed the PTO’s argument that the claimed nucleic acids lack the structure function relationship required by the Federal Circuit. Applicants have specified the structure of the claimed nucleic acid as those which hybridize to the complements of the specified sequences under the conditions detailed in the claims, and by amending the claims, have specified the function that is correlated to the structure. Applicants respectfully submit that the claims now closely track those of Example 9 of the Written Description Guidelines, where a claim to nucleic acids which hybridize to a disclosed sequence and retain a specific function were deemed to satisfy the written description requirement.

Applicants submit that the present case differs from the facts in *Regents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (Fed. Cir. 1997), where the gene was defined not by its structure, i.e. sequence, but rather by what it did. In *Lilly*, the claim was directed to a nucleic acid which “encodes insulin.” *Id.* at 1401. The Court characterized that claim as a “definition by function” since it merely describes the claimed nucleic acid by what it does – encodes insulin. *Id.* at 1406. Because nucleic acids which encode insulin were known to exist, but the claims at issue recited no structure, the Court held that “naming a type of material generally known to exist, *in the absence of knowledge as to what the material consist of*, is not a description of that material.” *Id.* at 1406 (emphasis added). The fact that the claims lacked any specific structure was important, and the Court distinguished the claims at issue from those which recited a specific DNA sequence. *Id.* n. 4 (“We note that in claims 4, 5, and 12-14 of the ‘740 patent [the claimed DNA] are described by reference to the structure of the claimed DNA sequences rather than by reference to their function.”).

Here, the claimed genus is defined not by its function, but by its structure – the claimed nucleic acids must possess a structure that is so similar to the disclosed sequences that it hybridizes under the specified conditions. As Examples 9 and 10 of the Written Description Guidelines make clear, specifying hybridization under highly stringent conditions yields “*structurally* similar DNAs,” not functionally similar DNAs. (Guidelines, Example 9 at page 36) (emphasis added). Thus, a hybridization limitation is a definition of structure, not function. For this reason, the present case differs from *Lilly*, where the nucleic acids were claimed only by their function.

Appl. No. : 10/033,167
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The instant case is also different from *Fiers v. Sugano*, 25 USPQ2d 1601. In that case, the Court held that in the absence of actual reduction to practice and disclosure of the entire DNA sequence, recitation of “its functional utility” (encoding a beta-interferon) was not sufficient to describe the DNA. *Id.* at 1604. Unlike *Fiers*, the gene in the instant case *has* been reduced to practice – the gene of SEQ ID NO: 6 has been cloned and sequenced. Therefore, the claimed nucleic acids are not being described merely by their “functional utility”.

Finally, Applicants submit that the PTO’s arguments regarding whether the disclosure of SEQ ID NOs: 6 and 7 are sufficient to describe the genus are moot in light of the current amendment adding a functional limitation to the claims. As Example 9 of the Written Description Guidelines makes clear, a single species is sufficient to describe a genus of nucleic acids which hybridize to the disclosed nucleic acid and retain the same function.

In conclusion, Applicants submit that they have satisfied the written description requirement by reducing the nucleic acid of SEQ ID NO: 6 to practice, by specifying the high stringency conditions under which hybridization occurs, and by requiring that the claimed nucleic acids possess the recited function which is related to their structure. As Example 9 of the Guidelines indicates, a claim to a genus of nucleic acids which hybridize to a disclosed sequence and possess a specific function is allowable. Thus, Applicants respectfully request that the PTO reconsider and withdraw its rejection of the pending claims under 35 U.S.C. § 112, first paragraph.

Appl. No. : 10/033,167
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CONCLUSION

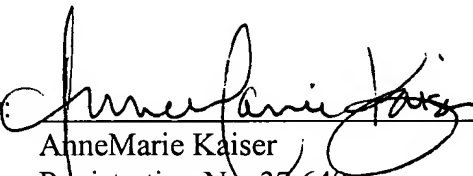
In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance. Nevertheless, the PTO is invited to contact the undersigned at the telephone number appearing below to discuss any remaining issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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